REMARKS

Claims pending are 1, 4-27, 29, 30, and 32-34. Per this response, new claims 35-37 are added to the application.

All claims as they existed prior to this response were rejected.

Claim Rejections:

1. Claims 1, 4-27, 29, 30, and 32-34 are rejected as not being enabled because, while it is acknowledged that the specification is enabling for providing a patient with a medication with an odorous marker additive and analyzing for the marker by way of electronic nose technology, the specification is said not to reasonably provide enablement for providing a patient with a medication comprising a combination of at least one active therapeutic agent and marker, which is not chemically part of the active therapeutic agent itself, and analyzing the breath utilizing an instrument adapted to detect the marker. It is asserted that the specification only provides enabling disclosure for the use of olfactory (odorous) markers and the use of electronic nose technology. It is asserted that the specification "does not provide support for the use of any sort of marker that is detected by any such instrument adapted to detect the marker, but rather only provides a "general narrative to the state of the art of many sensing technologies and generally discusses markers and medications, but does not relate all such elements and provide sufficient disclosure to show how such a method could be applied as currently claimed."

The ground for rejection is not understood, but to the extent that it is understood as discussed below, it is contested, and refuted.

First, the Examiner makes no showing that there is any distinction between what is conceded to be enabled, namely the use of odorous markers in combination with electronic nose technology, and the use of other markers which might not be "odorous" in the sense of giving off a smell that a human nose would detect. But the electronic nose technology does not detect "odorous" markers because such markers give off a smell that a human nose would detect.

Rather, such technology detects such markers by virtue of a specific response to the specific marker compound. This is no different than what is more broadly disclosed and claimed in this application.

Second, the specification is replete with disclosure teaching that the marker can be any marker, including but not limited to odorous markers, and the electronic sensor technology can be an electronic nose, but is not limited to such a device. See, for example, the Abstract of the disclosure:

> "The present invention includes a method and apparatus for monitoring drug compliance by **detecting markers, such as odors**, upon exhalation by a patient after medication is taken, wherein such markers result either directly from the medication itself or from an additive combined with the medication. In the case of olfactory markers, **the invention preferably utilizes electronic sensor technology**, such as the commercial devices referred to as "artificial noses" or "electronic noses," to non-invasively monitor compliance. The invention further includes a reporting system capable of tracking compliance (remote or proximate) and providing the necessary alerts."

The field of the invention recites:

> "[0003] The present invention relates to marker detection, in the form of **odors or the like**, to monitor drug compliance, and, more particularly, to a method and **apparatus for the detection of markers** wherein such markers are detectable either directly from the medication itself or from an additive combined with the medication and are detected upon exhalation after medication is taken by a patient."

This is not limited to odorous markers nor to electronic noses.

In the summary of the invention, it is taught:

"[0009] The present invention solves the needs in the art by providing a method and apparatus for monitoring drug compliance **by detecting markers, such as odors**, upon exhalation by a patient after medication is taken, wherein such markers result either directly from the medication itself or from an additive combined with the medication. **In the case of olfactory markers**, the invention **preferably utilizes electronic sensor technology, such as the commercial devices referred to as "artificial noses" or "electronic noses**," to non-invasively monitor compliance. The invention further includes a reporting system capable of tracking compliance (remote or proximate) and providing the necessary alerts."

Here it is taught that one might detect markers "such as odors", not exclusively odors, and that one may "preferably" utilize electronic sensor technology "such as …electronic noses" not exclusively electronic noses.

The summary continues:

"[0010] Therefore, it is an object of the present invention **to detect marker substances** as a measure of patient compliance **by methods including, but not limited to, sensor technology (e.g., silicon chip technology)** to non-invasively monitor compliance of patients to prescribed drug regimens."

Here, there is not even a mention of odor nor electronic noses – this is a specific object of the invention.

See also paragraph 0053 of the instant specification which makes it explicit that the current invention is not limited to the use of electronic nose technology.

"[0053] It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application and the scope of the appended claims. **Specifically, the**

marker detection method of the present invention is intended to cover detection not only through the exhalation by a patient with a device utilizing electronic nose technology, but also other suitable technologies, such as gas chromatography, transcutaneous/transdermal detection, semiconductive gas sensors, mass spectrometers, IR or UV or visible or fluorescence spectrophotometers. The invention also includes marker detection not only through a patient's exhaled breath, but also through sweat, saliva, urine, mucous, hair, nails, tears, and other bodily discharge of the patient."

This recitation of the teachings of the specification could continue, but it is considered sufficient here to remark that the specification is in no way limited, from a written description nor from an enablement point of view, to the use only of electronic noses or odorous materials. In any event, it is urged that it is incumbent on the Examiner to provide evidence as to why the applicant's invention is not enabled to the extent claimed, particularly in light of the Examiner's concession on the record that use of electronic noses and odorous markers for the designated and claimed purpose is enabled. What would prevent those of ordinary skill in the art to practice this invention to the full scope as claimed? It is urged that it is insufficient for the Examiner to make a generalized allegation in this regard. This issue was discussed at length with Examiner's Turk and Warden, and it is believed that the Examiner's acknowledged this point in the course of the 10 June 2009 interview. The disclosure that the marker may be a volatile organic compound, and that a wide range of sensors may be utilized in carrying out the novel method of the invention were also discussed, with citations to the application as published being made (e.g. see paragraphs 0018 to 0028 of the US20040081587 publication). Reconsideration and withdrawal of this ground for rejection is respectfully requested.

2. Claims 1, 4-27, 30, and 32-34 are rejected as failing to comply with the written description requirement, it being alleged that the claims contain new subject matter by virtue of the recitation that the medication comprises a combination of at least one therapeutic marker, which is not chemically part of the active therapeutic agent itself and where the combination is taken concurrently – it is alleged that the Applicant is drawing basis for such amended limitations from the disclosure of child application 11/097,647.

This is not correct, this is not new matter. While it is apparent that the Applicant in error did quote some supportive disclosure from the child application, in the previous response, the Applicant quoted extensively from disclosure which does, in fact, exist in the instant specification, to show support for the limitations included in the claims as they now stand pending. See pages 9-12 of the previous response, where it was asserted that:

> "The Abstract of the disclosure states that the "markers result either directly from the medication itself or from an additive combined with the medication." See likewise the disclosure at paragraph 0003, and 0017. Again, this cited disclosure is not the exclusive disclosure in the specification which makes it plain that the term "medication" includes the API, which itself may give rise to a detectable marker, or the marker may be a compound which is included with the API as part of "the medication". See also the legend of Figure 2, which states "PCMS includes marker compound included in medication that is exhaled into detection system for accurate and reliable monitoring off-site." See, likewise, the legend of Figure 3, which states: "Step 1 – Medication is taken, releasing Marker Compound". Likewise, for Figure 4, for which the legend states: "PCMS includes marker compound included in medication that is exhaled into detection system for accurate and reliable monitoring off-site." Thus, it is incorrect to state that the "currently recited method is not operable in detecting if the medication has/has not been taken as it only tests if the odorous marker has/has not been taken", as the marker is part of the medication, and according to the claim as herein amended, is taken concurrently with the therapeutic agent the adherence in taking of which is being monitored."

The cited written description comes from the instant specification, not from the daughter. The definition of the specific term "concurrent" may have inadvertently been recited from the daughter specification, (for which apologies are made here along with the assurance that such recitation was completely inadvertent and was made without any deceptive intent), but it is urged that this should be considered irrelevant in the sense that in the present specification, there is sufficient support in any event:

See the instant specification, for example, at paragraph 0045, which states:

> "0045] When **the drugs or drugs coated with selected markers are taken** (FIG. 2), the drugs are dissolved in the mouth (or digested in the stomach, transmitted to the lungs, etc.). The electronic nose can then detect the marker from the drugs or drugs coated with selected markers when the patient exhales (FIGS. 2 - 4) to confirm that the medication was taken on a dose by dose basis. The electronic nose can record and/or transmit the data sensed from the patient's breath for monitoring purposes."

If a drug is coated with the marker, there would be no way of taking the medication other than concurrently.

Likewise, at paragraph 0052 of the instant specification, it is described that:

"[0052] A further embodiment of the invention includes a communications device in the home (or other remote location) that will be interfaced to the electronic nose. The home communications device will be able to transmit immediately or at prescribed intervals directly or over a standard telephone line (or other communication means) the data collected by the compliance monitoring device. The communication of the data will allow the physician to be able to remotely verify if **the patient took the prescribed drug at the prescribed time and dose.** The data transmitted from the home can also be downloaded to a computer where the prescribed drug regimen is stored in a database, and any deviations within limits from the prescribed drug regimen would be automatically flagged (e.g., alarm) so that a home care nurse could telephone the patient and inquire about the reasons for deviating from the prescribed drug regimen."

This could not be the case unless, as the Examiner himself is asserting, and has been asserting in previous actions, the drug and the marker are taken concurrently – as otherwise there might not be the necessary nexus and association between the taking of the drug and the marker.

This is, after all, a significant purpose of the present invention and disclosure. It is urged that it would now be inequitable to forbid the Applicant to use a word to meet a rejection by the Examiner on the basis of which the claims are being amended in order to overcome the rejection (i.e. the need to limit the claim such that the required nexus existing between taking of the active agent and the marker) where the support is present in the specification to show the nexus and only an *ipsissimus verbis* recitation of a particular word helpful in describing that nexus is absent.

Further, claim 29 as originally filed read as follows:

"29. A method of producing medication which is detectable as an indication of patient compliance in taking the medication comprising the steps of: identifying a marker substance detectable in gaseous exhaled breath, and **producing a medication combined with said detectable marker substance,** said medication to be taken by volitional patient action at specified times whereby subsequent analysis of the patient's breath will confirm the presence of said marker substance and thus the patient's compliance in taking said medication."

Claim 9 as originally filed read:

"9. The method of claim 1 wherein the marker is an additive combined with the medication."

Again, these claims clearly describe, even if they do not use the word "concurrent" the combination of the marker with the medication such that concurrent taking of the active pharmaceutical agent and the marker substance occurs in order to document that the patient has taken the active medical agent at the prescribed time. It is urged that the specification provides explicit support on the basis of which the applicant should be entitled to use the word "concurrent" as a summary of what is described in the specification. It is urged that this disclosure in this application provides basis for the use of the specific term in the child application. Should the Examiner agree that the concept of concurrency is disclosed in the specification, but continue to object to the use of the specific word "concurrent" it is respectfully

requested that the Examiner consider a term that would be acceptable in light of all of the disclosure cited in the foregoing discussion.

With respect to claim 32, the Examiner specifically concedes that paragraph 0044 does provide support for the use of a combination of markers – which concession is gratefully acknowledged. Given this concession, however, it is therefore not understood why the previously presented argument in favour of support of this claim is stated to have been unpersuasive, even if, by error, the wrong specification was referred to – since this support in fact exists in both this specification and in the daughter specification?

In the course of the 10 June 2009 interview, this issue was discussed with Examiner's Turk and Warden. From that discussion, the undersigned came to understand that the concern over the use of the word "concurrent", at least as expressed by the Examiner's in that interview, is that inclusion of this term in the claim might indicate that there are separate "pots", one containing a marker and one containing the active therapeutic agent, and that it is necessary for the patient to imbibe both pots "concurrently". It was the Applicant's understanding from the discussion of this issue in the 10 June 2009 interview that, because the claim(s) include the word "combination" or "combined", it would be sufficient, in order to overcome this ground for objection/rejection to merely delete the term "concurrent" or "concurrently" from the claim(s). Therefore, notwithstanding the foregoing arguments and Applicant's position that the instant invention would operate even in the "two-pot" scenario, this amendment has been included herein without prejudice to Applicant's right to present such claims in a related or continuing application, in order to secure allowance of the claims as amended in this case. Reconsideration and withdrawal of this ground for rejection is appropriate and is respectfully requested.

3. Claim Rejections – 35 USC 103:

Claims 1, 8, 9, 12-20, 23-27, 29 and 32 are rejected as unpatentable over Kell (5,776,783) in view of Katzman (5,962,335).

The Examiner has kindly acknowledged that the 35 USC 102(e) rejection based on Katzman in the previous Office Action was not sustainable and has been withdrawn, because the Applicant's amendments and arguments on pages 9-25 of the response filed December 4th 2008 were persuasive. It is acknowledged and appreciated that the Examiner has confirmed that Katzman does not disclose that the medication comprises a combination of at least one active therapeutic agent and a marker, which is not chemically part of the active therapeutic agent itself.

On further consideration, however, the Examiner has reformulated the rejection using Kell as the primary and Katzman as the secondary reference, in a rejection based on 35 USC 103, rather than 102(e).

The Examiner acknowledges that Kell neither discloses nor suggests monitoring breath for purposes of confirming compliance in taking a medication – Kell is restricted to examination of urine. In addition, Kell is confined in its disclosure to monitoring compliance in taking a particular exemplified medication, namely methadone (column 7, line 57), with a particular exemplified compliance marker, namely a benzodiazepine – specifically required to be weakly acidic (see column 5, lines 1-4 of Kell and column 7, lines 4-15). Such a substance would not be volatile and would not be expected to appear on the breath. Further, the marker proposed by Kell must be provided at such a low level that it is therapeutically inert and so, even if it did appear on the breath, it would be in such vanishingly small quantities that it would not serve as a practical marker for compliance due to difficulties in reliable detection. Finally, Kell repeats (column 5, lines 27-34 and column 7, lines 27-37) that the prescribed marker has to have a long half life, of between about 24-48 hours so that it could be detected in urine. As a result, the immediacy of the method as taught by Kell (see column 15, lines 8-10 and column 15, lines 45-48) is severely compromised such that a lag of about 1 week is required, even if the patient is doubling or halving the amount of medication they should be taking, before the method according to Kell would detect such non-compliance. Accordingly, Kell does not teach a method which in any sense provides even an approximation of real-time readout of patient compliance in taking a particular dosage of a particular medication at a prescribed time.

In order to emphasize the distinction, therefore, between the instant invention and that which is disclosed in Kell, the present claims are hereby amended to reflect that the claimed method provides information "almost immediately" about the compliance or otherwise of the patient. That is, once the patient has taken a medication, as provided herein, which contains

combined therein a marker which appears rapidly in the breath, the feedback to the healthcare worker, patient themselves or any other individual with a need to confirm the compliance status of the patent, is very rapid. This is not new matter as support for this limitation is found throughout the specification and specifically, see paragraph 0037 of the 20040081787 publication of this application – which provides "Rapid detection after ingestion…". See also paragraph 0039 which provides "the invention detects the presence of that drug **almost immediately** in the exhaled breath of the patient…a non-toxic olfactory marker (e.g., volatile organic vapors added to the coating of the pill or in a separate fast dissolving compartment in the pill or the solution…will provide a method to determine if the drug was taken as prescribed." This element also relates to the ability of the instant invention to provide information about the compliance of the patient in taking the prescribed medication in the prescribed dose at the prescribed time.

It should be further noted that in Kell, the marker itself is an active pharmaceutical compound, as noted above, and therefore its concentration is required to be very low. By contrast, new claim 35 is introduced requiring that the maker is a compound that is Generally Recognized as Safe (i.e. a GRAS compound), which excludes compounds such as a benzodiazepine as taught by Kell.

It should also be noted that per Kell, a urine sample in order to be analyzed must be taken to a third party or laboratory. New claim 37 is introduced herein to emphasize this distinction. This is not new matter as paragraphs 0051 and 0052 of the application as published provide for in home or other remote location practice of the method.

Finally, as reflected in new claim 36 presented herein, the method of the present invention, because of its rapidity and ability to provide information about compliance or non-compliance in taking the medication, permits patients themselves to be apprised of their compliance or non-compliance status and if the status is non-compliant, this can be remedied almost immediately. This too is not new matter as paragraph 0011 includes alerting patients to their compliance status per this methodology and paragraph 0052 provides for, e.g. a home care nurse to telephone the patient and inquire about the reasons for deviating from the prescribed drug regimen. This, of course, is not possible using the methodology of Kell, wherein long lag times from taking a sample to deriving compliance information are inherent. It is urged that Katzman does not cure these deficiencies in the primary reference, Kell.

Katzman is cited for the proposition that it would have been obvious to combine its teaching with the teaching of Kell to arrive at the instant invention, where breath is measured to confirm compliance in taking a medication by monitoring breath, because Katzman teaches monitoring breath.

However, there are many problems with combining these two references, and the result of such a combination is not a disclosure or suggestion of the invention defined by the claims as herein amended.

First, Kell only discloses and discusses urine. As discussed above, with particular reference to Kell itself, urine does not provide a quick indication of therapeutic agent's ingestion, making it inadequate as a means to document compliance at the correct time by a patient required to take a medication at a particular dosage – there being a lag of about a week, per Kell itself, before compliance or non-compliance can be determined. Rather, compounds and metabolites of compounds excreted in the urine necessarily represent a significant time delay from the time of taking a medication and associated marker compounds to the time these compounds are excreted via the urine – passage from the blood, filtration by the kidneys, storage in the bladder, and finally release via the urine, all necessarily mean that there is a significant passage of time and averaging of metabolic processes, rather than an instantaneous or almost instantaneous readout of a particular time and dose – as is achieved by immediate transfer of compounds from the blood in the lungs to the exhaled breath per the current invention.

As has been extensively argued in relation to the 102(e) rejection based on Katzman, Katzman is not at all concerned with documenting compliance in taking medication. Rather, Katzman is concerned with monitoring the metabolism of an internally tagged (e.g. isotopically tagged) active therapeutic agent. This is distinguished in the present claims in that the marker is specifically limited herein to being a compound "which is not chemically part of the active therapeutic agent itself". In addition, in Katzman, there can be no doubt that the individual has taken the agent – if there were any doubt about this, the entire basis of Katzman's method would be in doubt. These arguments with respect to Katzman have been made on the record – see the previous response pages 17- 21. As noted there, the presently claimed invention has been modified to specifically recite that it is a method to determine **whether** a patient has taken a medication, and that Katzman has no relevance to such a situation at all. This is analogous to the distinction between, on the one hand, a method for determining **whether** a patient has cancer or

not and, on the other hand, a method for treating a patient with cancer. It would make no sense to argue that a method of treating a patient who is known to have cancer teaches anything at all about determining, in the first instance, **whether** the patient in fact has cancer or not. Therefore, the combination of Katzman with Kell can only be motivated by an improper hindsight reconstruction of what is disclosed and claimed in the present application, to thereby rationalize combining what is taught in Katzman (breath monitoring to measure metabolism of an active therapeutic agent having an internal isotopic marker) with the disclosure of Kell (having the completely different purpose of testing compliance in taking a medication, using urine as the means for testing with all of the attendant time delays and other deficits discussed above). The office has provided no rationale for why one skilled in the art aware of Kell would look to Katzman.

Even if the ordinarily skilled artisan were to encounter Kell and Katzman, by chance for example (as a search of the drug compliance literature and patents would not reveal Katzman - pertaining as it does, not to drug compliance monitoring, to methods for conducting metabolic studies of internally tagged compounds for which there can be no doubt that the test subjects have in fact taken the drug - if one were seeking to improve the method of Kell), then by looking at Kell and Katzman together, the ordinary artisan would conclude that if the goal were to measure compliance in taking a medication, one would need to create a new chemical entity with an internal label, as in Katzman, in order to apply that teaching to the field with which Kell was concerned for purposes of compliance monitoring by breath detection. This is specifically excluded from the present invention as claimed! Accordingly, the ordinarily skilled artisan would not be motivated to make this combination, and even if they did, they would end up with a process that is distinguishable from that which is disclosed and claimed in the present application. If the ordinary skilled artisan would not make this combination, neither should the USPTO.

In addition, reference is made here to paragraphs 0020 and 0029 of the application as published:

"Recent developments in the field of detection of marker substances include, but are not limited to, semiconductive gas sensors, mass spectrometers, IR or UV or visible or fluorescence spectrophotometers. The marker substances change the electrical properties of the semiconductors by making their electrical resistance vary, and the measurement of these

variations allows one to determine the concentration of marker substances. These methods and apparatus used for detecting marker substances use a relatively brief detection time, of around a few seconds, compared to those given by gas chromatography, which takes from several minutes to several hours."

"[0029] **The present invention will determine if a patient has taken the prescribed drug at the appropriate time and at the prescribed dosage** by monitoring and analyzing the exhaled gases with the electronic nose. In a preferred embodiment, the device of the present invention is designed so that patients can exhale via the mouth or nose directly into the device. The device is designed to detect the presence of medications and/or harmless olfactory markers added to medication (discussed hereinafter)."

The claims herein are amended to reflect the immediacy of the claimed method – such that detection if the patient has taken the prescribed medication at the prescribed time and in the prescribed dosage are positive limitations in the claims. This would not be possible by practicing Kell alone, with its inherent lag times, or even Kell in combination with Katzman, which requires detection of metabolites of an internally labelled therapeutically active agent.

In addition to paragraph 0029 of the specification quoted above, reference is also made to paragraph 0052 of the application as published, with emphasis by bolding being added:

"0052] A further embodiment of the invention includes a communications device in the home (or other remote location) that will be interfaced to the electronic nose. **The home communications device will be able to transmit immediately or at prescribed intervals directly or over a standard telephone line (or other communication means) the data collected by the compliance monitoring device**. The communication of the data will allow the physician to be able to remotely **verify if the patient took the prescribed drug at the prescribed time and dose.** The data transmitted from the home can also be downloaded to a computer where the prescribed drug regimen is stored in a database, and **any deviations within limits from the prescribed drug regimen would be automatically flagged (e.g., alarm) so that a home care nurse could telephone the patient and inquire about the reasons for deviating from the prescribed drug regimen.**"

If there were a delay of about a week, as per Kell, these requirements of the invention as disclosed and claimed herein could not be met. Katzman, although referring to breath, does not

disclose or suggest use of that method to in any immediate fashion, confirm compliance in taking a particular dose of a prescribed medication at a prescribed time. There is no motivation provided in either reference to combine its disclosure with the other reference, and even if this were done, the combination of the two references simply fails to disclose or suggest a system, as reflected in the instant claims, which in essentially real time permits the monitoring of compliance in taking prescribed medications at prescribed times by detecting a marker which had been taken in combination with the prescribed medication (and is not chemically part of the active therapeutic agent itself) and which would then rapidly appear in the patient's breath. The need for rapid detection has also been included in the claims to emphasize this requirement of the invention. The term "almost immediately" is included in the claims and this, clearly, on the record here being created, would apprise those skilled in the art and those in need of being apprised as to what comes within the scope of the claims, is intended to cover seconds and minutes and possibly even hours, but not days and weeks, as per the prior art (e.g. Kell) which is being distinguished by the inclusion of this term in the claims. Since Katzman involves delays to permit metabolism, and requires multiple samples to be taken in order to calculate such metabolic parameters as Cmax (maximum concentration of drug in breath) and Tmax (time to maximum concentration in breath), there is no teaching or suggestion of using breath to confirm compliance in taking any particular dosage at any particular time.

Reconsideration and withdrawal of this ground for rejection is therefore respectfully requested.

Claims 4, 5, and 21 are rejected as obvious over Kell in view of Katzman, as discussed above, and further in view of Payne WO98/39470.

The Examiner concedes that the Kell/Katzman combination does not disclose analyzing the patient's breath to confirm the presence of the marker by either semiconductor gas sensor technology or conductive polymer gas sensor technology, nor does this combination disclosure capturing the sample of the patient's breath in a vessel prior to analysis. Payne is cited to cure this acknowledged defect in the combined teaches of Kell/Katzman. However, even if it were conceded that Payne is adequate to cure that defect, and that it would be appropriate to make

such a combination (neither of which is conceded here), Payne does not cure the defects noted above in the combination of Kell/Katzman - i.e. that Katzman is not at all relevant to the field of compliance in taking a medication and Kell is only applicable to testing compliance by measuring urine, which does not provide the ability to test dose and time of taking a medication due to the averaged nature of drug levels excreted in urine. Payne is concerned with detection of conditions in a patient such as ketosis or halitosis, and teaches nothing about the adherence or otherwise to a medication regimen. Reconsideration and withdrawal of this ground for rejection is therefore appropriate.

Claims 6, 10, 11, and 34 are rejected as unpatentable over Kell/Katzman as discussed above, and further in view of Forester (4,762,719).

The Examiner concedes that Kell/Katzman does not teach that the marker is selected from the group as recited in claim 6, that the marker can be an odorous compound and can be provided as a coating on the medication, which may include a substance to stimulate salivation. These defects are said to be cured by the Forester reference.

However, as with the Payne reference, even if it is conceded that Forester does disclose these elements, this does not cure the essential defects in the Kell/Katzman reference as discussed above and applied to the claims from which these claims depend. Forester is concerned with, essentially, a candy, and teaches nothing about the adherence or otherwise to a medication regimen. Therefore, reconsideration and withdrawal of this ground for rejection is respectfully requested.

Claim 7 is rejected as being obvious in light of the Kell/Katzman combination as discussed above, and further in view of Guth 4,353,869. The Examiner concedes that the Kell/Katzman combination does not disclose use of a spectrophotometer, and Guth is recited for this element. However, even if Guth does provide these elements, Guth is concerned with an ampoule assembly holder, and in no way cures the above discussed defects in the Kell/Katzman combination of references. Reconsideration and withdrawal of this ground for rejection is respectfully requested.

Claim 22 is rejected as obvious in light of Kell/Katzman and further in view of Ueda, which is cited to cure the conceded absence in the Kell/Katzman combination of a disclosure of dehumidifying a sample of a patient's breath. Again, Ueda, even if it were conceded to provide this element, does not cure the basic defect in the Kell/Katzman combination as discussed above. Therefore, reconsideration and withdrawal of this ground for rejection is respectfully requested.

Claim 30 is rejected as obvious over Kell/Katzman as discussed above – even though it is conceded that the combined references do not teach transdermal administration. This rejection as to claim 30 suffers from the same defect as does this combination of references when applied to claim 1 from which claim 30 depends. Reconsideration and withdrawal of this ground for rejection is therefore respectfully requested.

Claim 33 is rejected as unpatentable over the Kell/Katzman combination, even though it is conceded that the combination does not teach more than one therapeutically active agent. It is stated that this is "seen as obvious, as Kelly/Katzman [sic. Kell/Katzman] is concerned with checking patient compliance in taking the medication, through detection of the added marker." However, as discussed above, Kell/Katzman does not operate for this purpose, given that Kell is only concerned with testing urine, which cannot provide information about time and dose, at least not in any degree of real-time nor with any degree of precision without having to back-calculate excretion rates and metabolism, all of which are averaged when urine is used for this purpose, and, in any event, Katzman is not applicable at all to the detection of whether a patient has or has not taken a medication, but requires this to be known before application of the Katzman method, which also requires that the medication itself be tagged so as to permit measurement of the metabolism rate of the active agent. Accordingly, reconsideration and withdrawal of this ground for rejection is appropriate.

4. Nonstatutory Obviousness-Type Double Patenting:

It is acknowledged that the Examiner is concerned that the claims in the present application and those in the daughter application USSN 11/097,647 might result in an

obviousness-type double patenting situation where claims of indistinguishable scope are presented in both that application and this application. Prosecution on the merits in the daughter application has only just begun, but it is urged that there already exist sufficient distinctions between the scope of the claims in this case and that case to obviate the concern in regard to obviousness type double patenting as between the claims in these two cases. Assuming that the response in this case resolves all other grounds for rejection, in order to achieve allowance in this case, the Applicant may either cancel claims in the daughter application which might form the basis of a double patenting rejection, or file a Terminal Disclaimer. It is respectfully requested that this concern be held in abeyance pending review of this response by the Examiner and review of the claims in the daughter application, with the understanding that one or the other of these options will be elected by the Applicant on an indication that the claims in this case would otherwise be allowable and that there remains a live obviousness type double patenting objection.

Conclusion:

As discussed in this amendment, it would not be appropriate to limit the instant claims by requiring use of odorous markers or olfactory markers and/or electronic noses, as the present disclosure enables those skilled in the art to practice this invention to its full scope using marker compounds detectible by use of appropriate sensors.

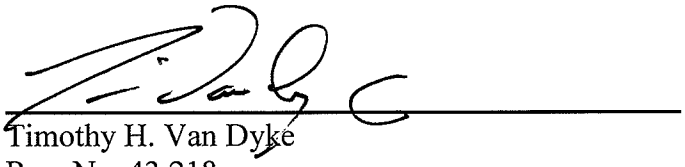
The word "concurrent" or "concurrently" has been removed from the claims as discussed with Examiners Turk and Warden in the 10 June 2009 interview, in favour of the "combined" limitation in the claims which conveys the nexus between the marker and the active agent included in the medication such that detection of the marker provides confirmation that the patient has taken the prescribed medication at the prescribed dosage and time.

The claims have been amended such that there are several limitations in the claims which, even if the combination of Kell and Katzman were appropriate, (which it is argued herein it is not and represents improper hindsight selection of references based on what is disclosed and claimed in this application), distinguish over the combination of Kell and Katzman. Likewise if the Ayer reference, cited in the daughter application, were joined to the obviousness rejection. These limitations include the requirement that the methodology rapidly ("almost immediately")

provide an indication of compliance, rather than accepting a long lag time, and that the method provide an indication that the patient has complied in taking the medication (including the marker) at the prescribed times and in the prescribed dosages. Kell does not permit this and Katzman, which in addition fails to meet the requirement of a marker that is not part of the active therapeutic agent, does not cure the defects in Kell, not least of which because in the first place, Katzman is not at all even concerned with the field of medication compliance. Ayer is also not concerned with the area of medication compliance and the constant osmotic delivery of medication from an implanted device, used as a surrogate for device operation, does not amount to a suggestion of a method for confirming patient volitional compliance in taking a presecribed medication in a prescribed dose and at a prescribed time. All of the remaining prior art rejections rely on the combination of Kell with Katzman and do not cure the essential defects in the combination of these primary references.

It is respectfully urged that all grounds for rejection of the claims in the present application have been addressed and overcome in this response. Should there be remaining issues of concern to the Examiner, the courtesy of a telephonic or in-person interview with the undersigned, in order to resolve any remaining concerns, is respectfully requested.

Respectfully submitted,



Timothy H. Van Dyke
Reg. No. 43,218
Beusse Wolter Sanks Mora & Maire P.A.
390 N. Orange Avenue, Suite 2500
Orlando, FL 32801
Phone: (407) 926-7726